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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/569,482

04/05/2006

Jun Takeuchi

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10/13/2009

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EXAMINER

MCDOWELL, BRIAN E

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

10/13/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/569,482	Applicant(s) TAKEUCHI ET AL.	
	Examiner BRIAN MCDOWELL	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 10 and 11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 10, 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

/BEM/

DETAILED ACTION

Status of Claims

Claims 1, 10, and 11 are pending in the instant application.

Priority

Applicant's submission of the appropriate English translated foreign priority documents, see Remarks, filed 8/11/2009, with respect to the Non-Final Office Action mailed 2/11/2009, has been fully considered. Thus, the instant application receives foreign priority to said documents.

Status of Specification and Claim Objections

Applicant's amendment of the specification and deletion of claims 12-14, see Remarks, filed 8/11/2009, with respect to the objection set forth in the Non-Final Office Action mailed 2/11/2009, have been fully considered and the objection has been overcome.

Status of Rejections

35 USC § 112 (2nd Paragraph)

Applicant's amendment of claim 1, see Remarks, filed 8/11/2009, with respect to the rejection set forth in the Non-Final Office Action mailed 2/11/2009, has been fully considered and the rejection has been overcome.

35 USC § 112 (1st Paragraph)

Applicant's amendment of claim 1, see Remarks, filed 8/11/2009, with respect to the rejection set forth in the Non-Final Office Action mailed 2/11/2009, has been fully considered and the rejection has been overcome.

New Objections and Rejections

Claim Objections

Claims 1, 10, and 11 are objected to because the instant claims possess non-elected subject matter. Applicant elected group I without traverse, *drawn to compounds of the general formula (I-X) seen in claim 5 and simple compositions thereof, where L = O, D = alkyl spacer (may be substituted), W = -OAlkyl (where alkyl spacer may be substituted), V = the spacer groups seen in claim 9, rings 1 and 2 = aryl, and the carbons that link N and L contain single bonds.*

For example, instant claim 1 recites W may be C1-alkylene and that rings 1 and 2 may be substituents other than "aryl" (e.g., pyridine or indan). The term "aryl" is viewed by one of ordinary skill in the art as fully aromatic carbocyclic compounds. Appropriate correction is required.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the aforementioned claim 1, applicant recites the limitation wherein ring 1 may be optionally substituted by a C1-10 straight or branched alkyl, alkenyl or alkynyl group, wherein optionally 1-2 of the carbon atoms may be replaced by oxygen, benzene, or a carbocyclic ring. If the substituent was a C1 alkyl and subsequently replaced by oxygen or any other ring, the resulting substituent would not be considered an "alkyl" group to one of ordinary skill in the art. The examiner currently can not define the metes and bounds of this particular limitation. Claims 10 and 11 depend on rejected claim 1 and are rejected.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts of the claimed compounds, does not reasonably provide enablement for N-oxides of said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

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Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444. Analysis is described below:

(A) Breadth of claims: The formula I-X is drawn to the instantly claimed compounds and their corresponding N-oxides that vary independently and lead to compounds of a wide variety of structures. These compounds encompass molecules that widely vary in physical and chemical properties such as size, molecular weight, acidity, basicity, and properties that are known in the art to greatly influence pharmacokinetic and pharmacodynamic parameters, not to mention the ability to productively bind to claimed biological target molecules. Thus, the claims are very broad.

(B) The nature of the invention: Benzoxazines of formula (I-X) (as well as N-oxides of said compounds) as agents for the treatment of respiratory diseases.

(C) State of the Prior Art: Chemistry is unpredictable. See *In Re Marzocchi and Horton* 169 USPQ at 367 paragraph 3:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of

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successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such workChemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)" Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

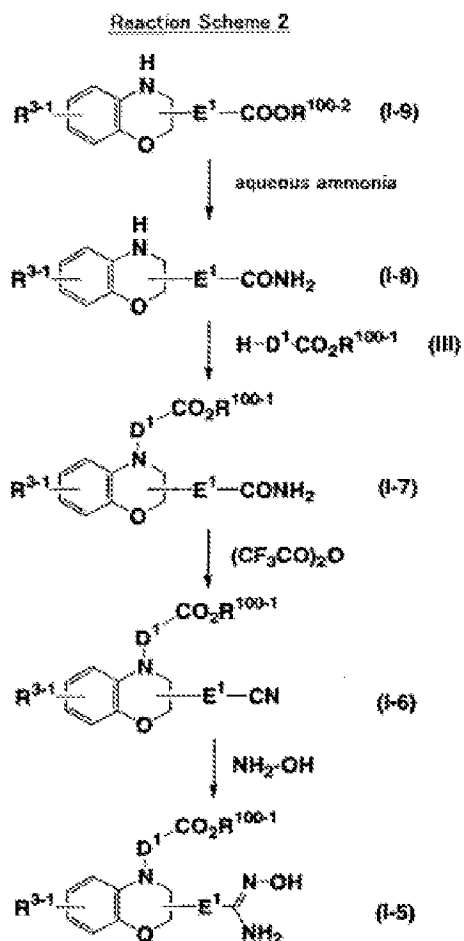
In addition, the examiner had not encountered any benzoxazines of similar structure from this particular field that contained the instantly claimed N-oxide functionality. N-oxides (more appropriately called "nitrones") are often utilized as starting materials in 1,3-dipolar cycloaddition reactions in the field of organic synthesis (Cary, F.A., and Sundberg, R.J. (2001), Advanced Organic Chemistry 4th Edition, New York: Kluwer Academic/Plenum Publishers).

(D) Skill of those in the art: The level of skill in the art is high and one would possess a Ph.D. in synthetic organic chemistry.

(E) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

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(F) Direction or Guidance: Little guidance or direction is provided by applicant in reference to making N-oxides of the instant invention. The instant disclosure only provides the vague synthetic scheme:



No where in the above scheme does applicant lead one of ordinary skill on how to obtain "N-oxides".

Due to the insufficient amount of guidance, one of ordinary skill would expect undue experimentation in obtaining N-oxides of the claimed compounds.

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(G) Working Examples: The compound core depicted with specific substituents represent a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed. Applicant has provided no working examples of any N-oxides of the formula I-X

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

(H) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome. Applicant fails to provide guidance and supporting information for making the thousands of other compounds which are encompassed by the claims, therefore undue experimentation would be expected.

Due to the level of unpredictability in the art, the very limited guidance provided, and the lack of working examples, the applicant has shown lack of enablement. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or

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use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN MCDOWELL whose telephone number is (571)270-5755. The examiner can normally be reached on Monday-Thursday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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